



Tetanus Adverse Event after VMMC for HIV Prevention in a Pre-circumcision Tetanus Immunized Male from Uganda: A Case Report

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Authors' contributions

This work was carried out in collaboration among all authors. Author EL developed the manuscript idea. Authors EL, AN, DB, HM and CW wrote the first draft of the manuscript. All the other authors contributed to subsequent versions. Author FKK managed the literature searches. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Background: Although tetanus is a life-threatening disease, its occurrence is rare in the post-vaccination era, especially in developed countries. The US President's Emergency Plan for AIDS Relief (PEPFAR) has supported scale up of Voluntary Medical Male Circumcision (VMMC) to reduce female-to-male HIV transmission in countries with a high prevalence of HIV. VMMC is generally safe, with less than 2% of clients experiencing moderate to severe adverse events. However, in most sub-Saharan countries with a high HIV prevalence and low male circumcision coverage, tetanus vaccination coverage among infants, especially male, remains suboptimal. This is a case report of a 45-year-old male who developed tetanus after pre-circumcision tetanus vaccination in a VMMC HIV/AIDS prevention intervention program in Uganda.

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The Case: A healthy 45-year-old male presented for voluntary circumcision at field VMMC centre. He received a standard pre-circumcision tetanus immunization and had no incident immediate post-operative. 14 days later he reported at a local health facility with a history of difficulty in swallowing, difficulty in breathing, loss of speech and was ultimately diagnosed with tetanus after 2 days. The patient was immediately admitted in intensive care unit, treated, improved and eventually discharged.

Conclusions: This report highlights the possibility of tetanus vaccine failure and importance of prompt diagnosis and treatment of tetanus. It also highlights the need for institution of aggressive quality improvement and pre-circumcision tetanus vaccination procedures. Post vaccination surveillance for possible vaccine failure is recommended in addition to a review of existing national immunization medical practice and policies.

Keywords: HIV; AIDS; vaccination; treatment; tetanus; adverse event; VMMC.

1. INTRODUCTION

Although tetanus is rare in the post-vaccination era in industrialized countries, it remains a life-threatening disease and important cause of death associated with a high case mortality in the developing world [1]. Emphasis on elimination of maternal and neonatal tetanus led to WHO global vaccination approaches that solely targeted women of reproductive age and infants [2-4]. Less attention has been given to male immunization after infancy yet the conferred immunity is not lifelong; and observed tetanus cases following Voluntary Medical Male Circumcision (VMMC) are emerging in different sub-Saharan African countries [5]. Thirteen tetanus cases were reported within 14 days following VMMC, eight of which resulted in death from programs that had conducted over 11 million procedures between April 2012 and end of 2015. These cases were reported from five of the 14 priority African countries identified for VMMC scale up including Uganda, Kenya, Rwanda, Zambia and Tanzania [5]. This followed the 2007 World Health Organization (WHO) and the Joint United Nations Program on HIV/AIDS (UNAIDS) pronouncement on VMMC as a key component of combination HIV prevention in countries with a high HIV prevalence and low levels of male circumcision [5].

1.1 Program Description

The URC Department of Defense HIV/AIDS Prevention Program (URC-DHAPP) implemented monthly mobile VMMC services to rapidly scale up VMMC throughout the country targeting soldiers, their families and surrounding communities. It is through this program that the subject voluntarily presented himself for circumcision at one of the centres in the field.

2. PRESENTATION OF CASE

A 45-year-old man was circumcised on August 8, 2019 at a district camp through a mobile voluntary male medical circumcision (VMMC) initiative in Buliisa district, Uganda. He was a fisherman working around Lake Albert. He was reported to have resumed fishing immediately after the circumcision procedure. A review of the VMMC records and interview with the circumcision team lead indicated that the procedure was done according to prescribed national standards. He received a pre-circumcision booster dose of 0.5 mL of Tetanus Toxoid (TT) administered prior to surgery on the same day and was issued a patient's TT card as evidence following the national protocols for pre-VMMC TT procedure. The protocols assume that residents received childhood tetanus vaccination as part of the national Diphtheria Pertussis and Tetanus (DPT) program; as such we were not required to ascertain a history of childhood DPT vaccination. The vaccines were stored using national cold chain systems. A post tetanus adverse event (AE) audit revealed that the cold chain was functional with temperatures within this particular cold chain maintained at the recommend standard through. The TT vaccine used was not expired, thus assumed to be potent.

2.1 Pre-Operation

The client was in good health, had no signs of urethral discharge, anatomical abnormalities, balanitis, surgical disorders, open wounds, or adhesions. His body temperature was 37°C, had a blood pressure of 120/72 mmHg, respiratory rate of 16BPM and weighed 56Kg. He was given a pre-surgical tetanus toxoid vaccine shot.

2.2 Surgery

The surgical site was cleaned with povidone iodine, injected with 5mls of lidocaine and 5mls of bupivacaine. The dorsal slit circumcision surgical technique was used, no adverse events occurred during and immediately after the operation. The procedure lasted 25 minutes.

2.3 48 Hours Follow Up

The patient returned to the health centre 12 hours post-operation complaining of discomfort due to a tight bandage. He was attended to by resident health workers at the local health centre. The dressing was changed, he reported no other adverse event signs such as bleeding, pus discharge, excessive swelling or failure to pass urine.

2.4 Post >48 Hours Period

Fourteen days after the procedure, he developed neck pain, dysarthria, dysphagia and difficulty in breathing. He was admitted at the local community health centre and treated with intravenous artesunate for malaria following a positive malaria rapid diagnostic test. The admitting clinician noted that he was unkempt and had soiled clothing on him. Four days later, Aug 24, 2019 (16 days post-operative) his condition worsened, he developed trismus which was reported as symptomatic for meningitis. He was immediately referred to the Regional Referral Hospital where a diagnosis of tetanus infection was made. On examination of the circumcision area, the wound was dry and almost completely healed. No other obvious wound was found on him as a likely entry point for the *Clostridium tetani*.

He was transferred to the National Referral Hospital in Kampala, the capital city, where he was isolated, given tetanus immunoglobulin, antibiotics and muscle relaxants, (tetanus toxoid vaccine, metronidazole, chlorpromazine and diazepam) for a period of five days. Despite the treatment, the spasms became more frequent, and although he remained fully conscious, he was unable to speak but was hemodynamically stable throughout that period.

2.5 ICU

The patient was transferred to an intensive care unit (ICU), conscious but critically ill, the spasms had worsened, he was incubated for feeding but

continued to breath normally without assisted ventilation. He was extremely drowsy but arousable, had generalized muscle rigidity and was unable to open his mouth. Two days later the spasms lessened and were classified as mild with about 3-5 unprovoked spasms per day, all his vital signs were normal. While in ICU he was treated with midazolam, diazepam, chlorpromazine a spasmolytic and received daily tetanus immunoglobulin and antibiotics.

Two weeks after admission the patient was discharged from hospital. He did not suffer major post tetanus motor sequelae except for remnant jaw stiffness for which he was advised to maintain jaw exercises to ease the trismus.

3. DISCUSSION

This is a case report of Tetanus infection following VMMC. Tetanus is an uncommon but severe disease that occurs predominantly among persons who are unvaccinated or inadequately vaccinated. Although vaccination against tetanus confers immunity, it is not lifelong and requires boosters at 10-year intervals [1]. Emerging male tetanus cases in sub-Saharan Africa following VMMC [5] amidst a heightened focus on maternal and neonatal tetanus vaccination [2-4] clearly indicates gender disparity in tetanus morbidity that inexplicably affects men. The nine African countries implementing VMMC which reported a post VMMC tetanus case, also had a low DPT3 coverage of less than 75% coverage in at least 2 years since 2000 [5]. None had a policy for vaccinating males against tetanus after infancy, indicating a population wide dearth of tetanus booster doses necessary for maintaining immunity against tetanus among males. There was no known history of previous tetanus toxoid vaccination in this patient, nor did the routine tetanus toxoid vaccination he was given prior to the VMMC intervention protect him against the disease, underscoring the need to change the current pre-VMMC tetanus toxoid protocols.

The primary contributor to tetanus cases in sub-Saharan Africa is un-vaccination or inadequate vaccination. It is unlikely that males receive the recommended primary 3-dose series of a tetanus toxoid-containing vaccine and a booster dose every 10 years which is effective in preventing tetanus or modifying its severity [6]. The low tetanus-toxoid vaccine coverage and limited WHO recommended fourth to sixth doses of tetanus vaccine for male adolescents and adults in African ought to be addressed to eliminate this emerging severe and often fatal infection among

men. Dalal et al recommend incorporation of a comprehensive tetanus vaccination approach in all VMMC programs as a priority [5]. Two tetanus-containing doses spaced 4 weeks apart for vaccine-naive individuals, with a further 2 week interval before the VMMC procedure. A booster dose at least seven, ideally 14 days before VMMC for individuals who are not fully vaccinated to induce partial immunity with an additional dose after the procedure to provide longer-term immunity.

The occurrence of tetanus in this patient could possibly be attributed to lack of sufficient protective tetanus antibodies immediately after the pre-operative TT vaccine. Makumbi et al found that 57% of men attending VMMC services in Uganda had insufficient immunity to tetanus, the prevalence of protective tetanus toxoid antibodies only increased rapidly after day 14 of the TT vaccine [7]. Other potential risk factors could have been attributed to HIV infection, older age (>40yrs), not having had a prior childhood DPT, malnutrition or having schistosomiasis infestations [8] although the patient was not investigated for presence of any of these ailments.

However at admission, our patient was unkempt and inspection of his home revealed an extremely dirty environment. He was also reported to draw potentially contaminated unclean water from the local unprotected stream for domestic use. Since the tetanus bacterium commonly resides in the environment; soil, dust and animal waste, the patient's unhygienic dwelling place was the most likely source of infection. A dirty environment and inappropriate

wound care practices which include application of home remedies that could be contaminated with *Clostridium tetani* spores presents a greater risk for infection for tetanus in all types of circumcision procedures [9]. VMMC programs must institute quality assurance standards including standard surgical protocols that emphasize a clean care approach for all circumcision methods, infection control, enhance proper individual and community post VMMC wound care, educate clients about hygiene, personal cleanliness and the risk of tetanus toxoid contaminants.

Although the incubation period of tetanus is 3 to 21 days, the shorter the period the higher the mortality risk [10], our patient presented on day 14, and this could partially explain his positive outcome. VMMC programs across Africa should institute adverse event postoperative tetanus surveillance systems to respond to emerging post-operative adverse events without delay. Since no laboratory tests can provide definitive diagnosis of tetanus, both VMMC recipients and peripheral community health facilities attendants should be sensitized and trained in the recognition of clinical presentation of tetanus.

High tetanus case fatality rates in Africa are mainly attributed to laryngospasm-associated respiratory failure, tetanus-associated autonomic dysfunction and lower quality of medical care at hospital settings according Woldeamanuel et al. [11]. This patient's chance of survival was enhanced by the immediate response to symptoms exhibited and an efficient referral system which enabled the regional referral hospital to make an accurate diagnosis.



Fig. 1. Left: Unprotected stream where patient bathed and sourced water for domestic use. Center: Inside patient's house, the mat served as his bed. Right: Entrance to his mud and wattle house. Photo credit: URC/UPDF staff

4. CONCLUSION

We reported a potential manifestation of TT vaccine failure, highlighted the importance of prompt tetanus diagnosis, treatment and need for institutionalization of aggressive quality improvement and pre-circumcision tetanus vaccination procedures. Institution of post vaccination surveillance for possible vaccine failure is recommended in addition to a thorough evaluation and review of existing national immunization medical practice to possibly include a 14 day post booster TT vaccine before VMMC surgery. VMMC programs should systematize personal and community education on appropriate wound care and personal hygiene. Since all circumcised men live within in the community, a proper referral network pathway needs to be instituted around circumcision camps to include training of health workers in the immediate recognition of tetanus symptoms, prompt care and referral mechanisms to intensive care units to minimize fatality in case of tetanus manifestation.

CONSENT

As per international or university standard, patients' written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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